9192.16USWO
Proposed New Claims

32. A polynucleotide comprising:
(i) a construct comprising at least three hypoxia response elements (HRE) operably linked to a promoter;
(ii) a nucleic acid sequence encoding HIF-1, endothelial PAS domain protein (EPAS), or both, operably linked to the construct; and
(iii) one or more nucleic acid sequence of interest (NOI) operably linked to the construct.

33. The polynucleotide of claim 32, wherein the promoter is selected from an SV4O promoter or an MLV promoter.

34. The polynucleotide of claim 32, wherein each of the HREs comprises at least one HIF-1 binding site and wherein each of the HIF-1 binding sites comprises the nucleotide sequence CGTG.

35. The polynucleotide of claim 32, wherein the HREs are direct repeats.

36. The polynucleotide of claim 34, wherein one or more of the HREs comprises a phosphoglycerate kinase (PGK) HRE.

37. The polynucleotide of claim 34 wherein the PGK HRE comprises the nucleic acid sequence of SEQ ID NO:1 or SEQ ID NO:2.

38. The polynucleotide of claim 34, wherein one or more of the HREs comprises erythropoietin (EPO) HRE, LDH HRE, glucose trpt HRE, vascular endothelial cell growth factor (VEGF) HRE, NOS HRE, aldolase HRE, enolase HRE, or heme oxygenase HRE.

39. The polynucleotide of claim 34, wherein one or more of the HREs comprises the nucleic acid sequence of SEQ ID NO:12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, or 23.

40. The polynucleotide of claim 32, wherein at least one of the HREs is a mutant HRE having reduced HIF binding activity.

41. The polynucleotide of claim 33, comprising at least four HREs linked to the promoter, wherein at least two of the HREs are positioned upstream (5') of the promoter and at least two of the HREs are positioned downstream (3') of the promoter.

42. The polynucleotide of claim 41, comprising at least six HREs, wherein at least three HREs are positioned upstream (5') of the promoter and at least three HREs are positioned downstream (3') of the promoter.

43. The polynucleotide of claim 42, wherein at least three of the HREs are phosphoglycerate kinase (PGK) HREs operably linked to an SV40 promoter or an MLV promoter.

44. The polynucleotide of claim 43, adapted to deliver the NOI to a mammalian cell.

45. The polynucleotide of claim 32, disposed in a nucleic acid vector.

46. The polynucleotide of claim 45, wherein the vector is a viral vector.

47. The polynucleotide of claim 46, wherein the viral vector further comprises:
(i) a nucleotide sequence encoding an inhibitory RNA molecule capable of affecting the cleavage, directly or indirectly, of VHL RNA;
(ii) one or more inhibitory RNA molecules that binds to and prevents VHL RNA processing, expression, or both; or
(iii) a nucleotide sequence encoding a polypeptide capable of inhibiting the binding of VHL to Elongin B, Elongin C, or both.

48. The polynucleotide of claim 47, wherein said nucleotide sequence (iii) encodes a non-functional derivative of wild-type VHL.

49. The polynucleotide of claim 46, wherein the viral vector is a retroviral vector.

50. The polynucleotide of claim 46, wherein the viral vector is an adenoviral vector.

51. The polynucleotide of claim 46, wherein the viral vector is a lentiviral vector.

52. A method of producing a viral strain comprising introducing a polynucleotide of claim 33 into the genome of a virus.